Applicants: Sprecher et al. Serial No.: 09/892,949 Filed: June 26, 2001

For: CYTOKINE RECEPTOR ZCYTOR17

# In the Claims

Please amend claims 1, 3-5, 16 and 17.

Per 37 C.F.R. §1.121, the current status of all the claims in the present application is presented below, amended claims are notated to indicated changes made (underlining additions and striking-through deletions) and the text of pending claims not being amended are presented clean.

Claim 1 (currently amended): An isolated polynucleotide <u>encoding a polypeptide</u>, wherein the <u>encoded</u> polypeptide comprises a sequence of amino acid residues that is selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);
- (c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);
- (d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);
- (e) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val);
- (g) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile);
- (h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 732 (Val); and
- (i) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 1 (Met) to amino acid number 649 (Ile).

Claim 2 (original): An isolated polynucleotide comprising a sequence selected from the group consisting of:



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(a) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 851;

(b) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 1727;

(c) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 1799;

(d) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 1800 to amino acid number 2366;

(e) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 1791 to amino acid number 2108;

(f) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 228 to amino acid number 2366;

(g) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 219 to amino acid number 2108;

(h) a polynucleotide as shown in SEQ ID NO:1 from nucleotide number 171 to amino acid number 2366;

(i) a polynucleotide as shown in SEQ ID NO:45 from nucleotide number 162 to amino acid number 2108; and

(j) a polynucleotide sequence complementary to (a) through (i).

Claim 3 (currently amended): An isolated polynucleotide according to claim 1, wherein the <u>encoded</u> polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

Claim 4 (currently amended): An isolated polynucleotide according to claim 1, wherein the <u>encoded</u> polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2 or 544 (Lys) to 649 (Ile) of SEQ ID NO:46.

Claim 5 (currently amended): An isolated polynucleotide according to claim 1, wherein the <u>encoded</u> polypeptide <u>encoded</u> by the <u>polynucleotide</u> has activity as measured by cell



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proliferation, activation of transcription of a reporter gene, or wherein the <u>encoded</u> polypeptide <u>encoded</u> by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids selected from the group consisting of:

(a) the polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ

ID NO:2;

(b) the polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ

ID NO:2;

(c) the polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ

ID NO:2;

(d) the polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ

ID NO:2;

(e) the polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ

ID NO:46;

(f) the polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ

ID NO:2;

(g) the polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ

ID NO:46;

(h) the polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ

ID NO:2; and

(i) the polypeptide comprising amino acid number 1 (Met) to 649 (Ile) of SEQ ID

NO:46, and

wherein the binding of the antibody to the isolated polypeptide is measured by a biological or biochemical assay including radioimmunoassay, radioimmuno-precipitation, Western blot, or enzyme-linked immunosorbent assay.

Claim 6 (original): An expression vector comprising the following operably linked elements:

a transcription promoter;

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a DNA segment encoding a polypeptide comprising an amino acid sequence a

a DNA segment encoding a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 732 (Val) or an amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to 649 (Ile); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

Claim 7 (original): An expression vector according to claim 6, further comprising a secretory signal sequence operably linked to the DNA segment.

Claim 8 (original): A cultured cell comprising an expression vector according to claim 7, wherein the cell expresses a polypeptide encoded by the DNA segment.

Claim 9 (original): An expression vector according to claim 6, wherein the DNA segment encodes a polypeptide comprising an amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 227 (Pro); or as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to 519 (Glu); and

a transcription terminator,

wherein the promoter, DNA segment, and terminator are operably linked.

Claim 10 (original): An expression vector according to claim 9, further comprising a secretory signal sequence operably linked to the DNA segment.

Claim 11 (original): An expression vector according to claim 9, wherein the polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

Claim 12 (original): An expression vector according to claim 9 wherein the polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2, or residues 544 (Lys) to 649 (Ile) of SEQ ID NO:46.



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Claim 13 (original): A cultured cell into which has been introduced an expression vector according to claim 9, wherein the cell expresses a soluble receptor polypeptide encoded by the DNA segment.

Claim 14 (original): A DNA construct encoding a fusion protein, the DNA construct comprising:

a first DNA segment encoding a polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

- (a) the amino acid sequence of SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 19 (Ala);
- (b) the amino acid sequence of SEQ ID NO:54 from amino acid number 1 (Met), to amino acid number 32 (Ala);
- (c) the amino acid sequence of SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 227 (Pro);
- (d) the amino acid sequence of SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 519 (Glu);
- (e) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 520 (Ile) to amino acid number 543 (Leu);
- (g) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);
- (h) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);
- (i) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val); and
- (j) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile); and

at least one other DNA segment encoding an additional polypeptide, wherein the first and other DNA segments are connected in-frame; and wherein the first and other DNA segments encode the fusion protein.



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Claim 15 (original): An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA construct encoding a fusion protein according to claim 14; and

a transcription terminator,

wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

Claim 16 (currently amended): A cultured cell comprising an expression vector according to claim 15, wherein the cell expresses a polypeptide the fusion protein encoded by the DNA construct.

Claim 17 (currently amended): A method of producing a fusion protein comprising:

culturing a cell according to claim 16; and isolating the polypeptide fusion protein produced by the cell.

Claim 18 (original): An isolated polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);
- (c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 543 (Leu);
- (d) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 544 (Lys) to amino acid number 732 (Val);
- (e) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 544 (Lys) to amino acid number 649 (Ile);
- (f) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 732 (Val);



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(g) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 20 (Ala) to amino acid number 649 (Ile);

- (h) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met) to amino acid number 732 (Val); and
- (i) the amino acid sequence as shown in SEQ ID NO:46 from amino acid number 1 (Met) to amino acid number 649 (Ile).

Claim 19 (original): An isolated polypeptide according to claim 18, wherein the polypeptide further comprises a transmembrane domain consisting of residues 520 (Ile) to 543 (Leu) of SEQ ID NO:2.

Claim 20 (original): An isolated polypeptide according to claim 18 wherein the polypeptide further comprises an intracellular domain consisting of residues 544 (Lys) to 732 (Val) of SEQ ID NO:2 or 544 (Lys) to 649 (Ile) of SEQ ID NO:46.

Claim 21 (original): An isolated polynucleotide according to claim 18 wherein the polypeptide has activity as measured by cell proliferation, activation of transcription of a reporter gene, or wherein the polypeptide encoded by the polynucleotide further binds to an antibody,

wherein the antibody is raised to a polypeptide comprising a sequence of amino acids from the group consisting of:

- (a) the polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ
- ID NO:2;
- (b) the polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ
- ID NO:2:
- (c) the polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ
- ID NO:2;
- (d) the polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ
- ID NO:2;
- (e) the polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ

ID NO:46;



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(f) the networkide commission amine said number 20 (Ale) to 722 (Val) of SEC

(f) the polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ

ID NO:2;

(g) the polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ

ID NO:46;

(h) the polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ

ID NO:2; and

(i) the polypeptide comprising amino acid number 1 (Met) to 649 (Ile) of SEQ ID

NO:46, and

wherein the binding of the antibody to the isolated polypeptide is measured by a biological or biochemical assay including radioimmunoassay, radioimmuno-precipitation, Western blot, or enzyme-linked immunosorbent assay.

Claim 22 (original): A method of producing a polypeptide comprising: culturing a cell according to claim 8; and isolating the polypeptide produced by the cell.

Claim 23 (original): An isolated polypeptide comprising an amino acid segment selected from the group consisting of:

- (a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);
- (b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);
  - (c) the amino acid sequence as shown in SEQ ID NO:18; and
  - (d) the amino acid sequence as shown in SEQ ID NO:22,

wherein the polypeptide is substantially free of transmembrane and intracellular domains ordinarily associated with hematopoietic receptors.

Claim 24 (original): A method of producing a polypeptide comprising: culturing a cell according to claim 13; and isolating the polypeptide produced by the cell.

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comprising:

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Claim 25 (original): A method of producing an antibody to a polypeptide

inoculating an animal with a polypeptide selected from the group consisting of:

- (a) a polypeptide consisting of 9 to 713 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:2 from amino acid number 20 (Ala), to amino acid number 732 (Val);
- (b) a polypeptide consisting of 9 to 630 amino acids, wherein the polypeptide comprises a contiguous sequence of amino acids in SEQ ID NO:46 from amino acid number 20 (Ala), to amino acid number 649 (Ile);
- (c) a polypeptide comprising amino acid number 20 (Ala) to 227 (Pro) of SEQ ID NO:2;
- (d) a polypeptide comprising amino acid number 20 (Ala) to 519 (Glu) of SEQ ID NO:2;
  - (e) a polypeptide comprising amino acid number 20 (Ala) to 543 (Leu) of SEQ ID
  - (f) a polypeptide comprising amino acid number 544 (Lys) to 732 (Val) of SEQ

ID NO:2;

NO:2;

(g) a polypeptide comprising amino acid number 544 (Lys) to 649 (Ile) of SEQ

ID NO:46;

(h) a polypeptide comprising amino acid number 20 (Ala) to 732 (Val) of SEQ ID

NO:2;

(i) a polypeptide comprising amino acid number 20 (Ala) to 649 (Ile) of SEQ ID

NO:46;

(j) a polypeptide comprising amino acid number 1 (Met) to 732 (Val) of SEQ ID

NO:2;

(k) a polypeptide comprising amino acid number 1 (Met) to 649 (Ile) of SEQ ID

NO:46,

- (l) a polypeptide comprising amino acid residues 43 through 48 of SEQ ID NO:2;
- (m) a polypeptide comprising amino acid residues 157 through 162 of SEQ ID

NO:2;

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(n) a polypeptide comprising amino acid residues 158 through 163 of SEQ ID NO:2;

(o) a polypeptide comprising amino acid residues 221 through 226 of SEO ID

NO:2; and

(p) a polypeptide comprising amino acid residues 426 through 431 of SEQ ID

NO:2; and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

Claim 26 (original): An antibody produced by the method of claim 25, which specifically binds to a polypeptide of SEQ ID NO:2 or SEQ ID NO:46.

Claim 27 (original): The antibody of claim 26, wherein the antibody is a monoclonal antibody.

Claim 28 (original): An antibody that specifically binds to a polypeptide of claim 18.

Claim 29 (original): A method of detecting, in a test sample, the presence of a modulator of cytokine receptor protein activity, comprising:

culturing a cell into which has been introduced an expression vector according to claim 9, wherein the cell expresses the protein encoded by the DNA segment in the presence and absence of a test sample; and

comparing levels of activity of the protein in the presence and absence of a test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of modulator of the protein activity in the test sample.

Claim 30 (original): A method for detecting a cytokine receptor ligand within a test sample, comprising:



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contacting a test sample with a polypeptide comprising an amino acid sequence from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 227 (Pro);

(b) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 20 (Ala) to amino acid number 519 (Glu);

(e) the amino acid sequence as shown in SEQ ID NO:18; the amino acid sequence as shown in SEQ ID NO:22; and detecting the binding of the polypeptide to a ligand in the sample.

Claim 31 (original): A method according to claim 30 wherein the polypeptide is membrane bound within a cultured cell, and the detecting step comprises measuring a biological response in the cultured cell.

Claim 32 (original): A method according to claim 31 wherein the biological response is cell proliferation or activation of transcription of a reporter gene.

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